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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,915	11/28/2000	Naoki Nakayama	99,569-A	8656

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EXAMINER
ROMEO, DAVID S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/724,915	Applicant(s) NAKAYAMA ET AL.	
	Examiner David S Romeo	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *9,12-44 and 46-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,11 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-56* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5, 6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-56 are pending.

Applicant's election with traverse of group I, claims 1-8, 10, 11, 45, and the species SEQ ID NO: 7 in Paper No. 11 is acknowledged. The traversal is on the ground(s) that it would not be an undue hardship to search SEQ ID NO: 7 and SEQ ID NO: 11. This is not found persuasive because an application may properly be required to be restricted to one of two or more claimed invention if they are able to support separate patents and they are either independent (MPEP § 806.04 - § 806.04 (j)) or distinct (MPEP § 806.05 - § 806.05(i)). SEQ ID NO: 7 and SEQ ID NO: 11 are distinct for the reasons given in the Office action mailed July 2, 2002 (Paper No. 9). Furthermore, SEQ ID NO: 7 and SEQ ID NO: 11, in spite of their similarity, are structurally distinct molecules and require separate searches of the literature and sequence databases and would therefore present an undue search burden. Furthermore, for each SEQ ID NO: there are three independent claims. For each independent claim there are at least 5, 6, and 8 Markush members. Therefore, for each SEQ ID NO: there are at least 5 x 6 x 8 = 240 considerations. To examine SEQ ID NO: 7 and 11 together is to increase this burden two-fold.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9, 12-44, 46-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

It is noted that in the restriction mailed July 2, 2002 (Paper No. 9), Applicants were notified that the restriction between the four sequences is not a requirement for an election of species but is rather a further requirement for restriction among independent and distinct inventions, and Applicants were required to elect one from A-D. In response Applicants elected SEQ ID NO: 7. Insofar as SEQ ID NO: 7 encodes SEQ ID NO: 8, Applicants' election of SEQ ID NO: 7 has been construed as a constructive election of C, nucleic acid molecules encoding the polypeptide of SEQ ID NO: 8. Claims 1-8, 10, 11, 45 are being examined only to the extent that they read upon nucleic acid molecules encoding the polypeptide of SEQ ID NO: 8.

Applicant's election of the species BLASTN in Paper No. 14 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim 11 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) to the extent that it is drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 14.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-8, 10, 11, 45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the deposit of the ATCC Deposit No. that corresponds to SEQ ID NO:. While the specification provides enough information for one of skill in the art to produce a polynucleotide comprising a coding sequence with the same or similar properties as, reproduction of an identical polynucleotide is a highly unpredictable event. Because it does not appear that the ATCC Deposit No. that corresponds to SEQ ID NO: 7 is known and publicly available or can be reproducibly isolated form nature without undue experimentation and because the claims require the use of the ATCC Deposit No. that corresponds to SEQ ID NO: 7, a suitable deposit of the clones is required for patent purposes.

Applicants referral to the deposit of the ATCC Deposit No. that corresponds to SEQ ID NO: 7 at page 92 is insufficient to ensure that all of the conditions of 37 CFR § 1.801-1.809 have been met.

If the deposit was made under the provision of the Budapest Treaty, filing of an affidavit or declaration by applicants or assignees, or a statement by an attorney of record over his or her signature and registration number, stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this

application and that the deposit will be replaced if viable samples cannot be dispensed by the depository, is required. This requirement is necessary when a deposit is made under the provisions of the Budapest Treaty as the treaty leaves these specific matters to the discretion of each State. Amendment of the specification to recite the date of the deposit and the complete name and address of the depository, and amendment of the claims to refer to the accession number, is required. In addition, claims reciting the deposited material must be amended to include the depository accession number of the deposited material.

Furthermore, unless the deposit was made at or before the time of filing, a declaration under 37 CFR 1.132 is necessary to construct a chain of custody. The declaration, executed by a person in a position to know, should identify the deposited clones by its depository accession number, establish that the deposited clones are the same as that described in the specification and establish that the deposited clone was in applicants' possession at the time of filing.

The new address for the ATCC, effective March 23, 1998, is American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209.

Claims 1-8, 10, 11, 45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The present specification discloses polynucleotides encoding the amino acid sequence of SEQ ID NO: 8 and exemplifies such a polynucleotide with SEQ ID NO: 7. The claims are directed to or encompass nucleic acid molecules that hybridize to the complement of such polynucleotides, or to polynucleotide variants of such polynucleotides,

or to polynucleotides encoding variants of SEQ ID NO: 8; nucleic acid molecules encoding a polypeptide having a percent identity to the amino acid sequence of SEQ ID NO: 8; nucleic acid molecules comprising allelic or splice variants of polynucleotides encoding SEQ ID NO: 8, or other variants of polynucleotides encoding variants of SEQ ID NO: 8; nucleic acid molecules comprising fragments of polynucleotides encoding fragments of SEQ ID NO: 8; nucleic acid molecules encoding conservatively or non-conservatively amino acid substituted, inserted, or deleted variants of SEQ ID NO: 8. This rejection is meant to encompass any and/or all embodiments of the claims other than a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 7 or the nucleotide sequence of the insert of the deposited clone that corresponds to SEQ ID NO: 7, or a nucleic acid molecule encoding the amino acid sequence of SEQ ID NO: 8 or the amino acid sequence encoded by the deposited clone that corresponds to SEQ ID NO: 7.

In some instances the claims require that the polypeptide encoded by the claimed nucleic acid molecule possess an activity that is possessed by the polypeptide of SEQ ID NO: 8 or possess antigenic properties. However, the claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Simply describing a large genus of any and/or all potential activities, as in, "an activity that is possessed by the polypeptide of SEQ ID NO: 8", is not sufficient to satisfy the written description requirement as to a particular biological activity. Nor does such a description lead those skilled in the art to a particular activity. The property of being "antigenic" says nothing regarding the particular antigenicity of the polypeptide or fragment. Thus, the claims are drawn to a genus of nucleic acid molecules encoding a genus of variant polypeptides

that is specifically defined only by some level of nucleotide or amino acid sequence similarity. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. In some cases, the specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO: 8. In some cases, the specification and claim do not place any limit on the number of nucleotide substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO: 7 or to polynucleotides encoding SEQ ID NO: 8. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus and because the genus is highly variant, SEQ ID NO: 7 and polynucleotides encoding SEQ ID NO: 8, alone, are insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim

is a partial structure in the form of some level of amino acid or nucleotide sequence identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed. The specification does not clearly allow persons of ordinary skill in the art to recognize that Applicants invented what is claimed. The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides and/or polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of making or isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating or making it. The compound itself is required. One cannot describe what one has not conceived. Therefore, only nucleic acid molecules comprising the nucleotide sequence of SEQ ID NO: 7 or nucleic acid molecules encoding the amino acid sequence of SEQ ID NO: 8, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

Claims 1-8, 10, 11, 45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. .

The claims are directed to or encompass nucleic acid molecules that hybridize to the complement of such polynucleotides, or to polynucleotide variants of such polynucleotides, or to polynucleotides encoding variants of SEQ ID NO: 8; nucleic acid molecules encoding a polypeptide having a percent identity to the amino acid sequence of SEQ ID NO: 8; nucleic acid molecules comprising allelic or splice variants of polynucleotides encoding SEQ ID NO: 8, or other variants of polynucleotides encoding variants of SEQ ID NO: 8; nucleic acid molecules comprising fragments of polynucleotides encoding fragments of SEQ ID NO: 8; nucleic acid molecules encoding conservatively or non-conservatively amino acid substituted, inserted, or deleted variants of SEQ ID NO: 8. This rejection is meant to encompass any and/or all embodiments of the claims other than a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 7 or the nucleotide sequence of the insert of the deposited clone that corresponds to SEQ ID NO: 7, or a nucleic acid molecule encoding the amino acid sequence of SEQ ID NO: 8 or the amino acid sequence encoded by the deposited clone that corresponds to SEQ ID NO: 7. In some instances the claims require that the polypeptide encoded by the claimed nucleic acid molecule possess an activity that is possessed by the polypeptide of SEQ ID NO: 8 or possess antigenic properties. However, the claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Simply describing a large genus of any and/or all potential activities, as in, "an activity that is possessed by the polypeptide of SEQ ID NO: 8", is not sufficient to describe a particular biological activity. Nor does such a description lead those

skilled in the art to a particular activity. The property of being "antigenic" says nothing regarding the particular antigenicity of the polypeptide or fragment. Furthermore, there are no working examples of such variant polynucleotides and polypeptides possessing any and/or all activities encompassed by "an activity". The specification lacks guidance for the amino acids in SEQ ID NO: 2 that are essential for "an activity" and structural integrity and those amino acids that are either expendable or substitutable. The skilled artisan is left to extensive experimentation wherein such variant polynucleotides and polypeptides are randomly made and through trial and error experimentation is left to determine how such variants can be used. Moreover, there is a lack of predictability in the art. Predicting structure, hence function, from primary amino acid sequence data is extremely complex and there doesn't exist an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. See Bowie (w8) page 1306, column 1, full paragraph 1, or Ngo (x8) page 433, full paragraph 1, and page 492, full paragraph 2.

In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-8, 10, 11, 45 are indefinite over the recitation of "moderately or highly stringent conditions" because stringency varies according to the hybridization conditions and the particular hybrid under study. The specification fails to precisely define "moderately or highly stringent conditions". One of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. The metes and bounds are not clearly set forth.

Claims 8, 10 are indefinite because they recite the term "CHL polypeptide". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "CHL polypeptide" an artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claims 2-8, 10, 11, 45 are indefinite over the recitation of "an activity" of the polypeptide set forth in SEQ ID NO: 8. Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "an activity" an artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth. It is unclear what activity is intended.

Claims 1-8, 10, 11, 45 are indefinite over the recitation of "complementary to" because it is unclear if a nucleotide sequence that is a full length complement or a nucleotide sequence that is only complementary to some portion of a nucleic acid molecule is intended. The metes and bounds are not clearly set forth.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 11 are rejected under 35 U.S.C. 102(a) as being anticipated by IMAGE clone 1857913, as evidenced by NCI-CGAP (u13) and The I.M.A.G.E. Consortium (v13).

NCI-CGAP (u13) discloses that IMAGE clone 1857913 is an isolated nucleic acid molecule comprising a nucleotide sequence that is 99.7% identical to nucleotides 734 - 1088 of the present application's SEQ ID NO: 7, as indicated below:

```
AI246227/c
LOCUS       AI246227                355 bp    mRNA    linear   EST 28-JAN-1999
DEFINITION  qi29f01.x1 Soares_NhHMPu_S1 Homo sapiens cDNA clone IMAGE:1857913
            3', mRNA sequence.
ACCESSION   AI246227
VERSION     AI246227.1  GI:3841624
KEYWORDS    EST.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 355)
  AUTHORS   NCI-CGAP http://www.ncbi.nlm.nih.gov/ncicgap.
  TITLE     National Cancer Institute, Cancer Genome Anatomy Project (CGAP),
            Tumor Gene Index
  JOURNAL   Unpublished (1997)
COMMENT     Contact: Robert Strausberg, Ph.D.
            Email: cgapbs-r@mail.nih.gov
            This clone is available royalty-free through LLNL ; contact the
            IMAGE Consortium (info@image.llnl.gov) for further information.
            Insert Length: 710   Std Error: 0.00
            Seq primer: -40UP from Gibco
            High quality sequence stop: 263.
FEATURES             Location/Qualifiers
     source          1. .355
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /clone="IMAGE:1857913"
                     /clone_lib="Soares_NhHMPu_S1"
                     /tissue_type="Pooled human melanocyte, fetal heart, and
                     pregnant uterus"
                     /lab_host="DH10B"
                     /note="Organ: mixed (see below); Vector: pT7T3D-Pac
                     (Pharmacia) with a modified polylinker; Site_1: Not I;
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                     Site_2: Eco RI; Equal amounts of plasmid DNA from three
                     normalized libraries (melanocyte 2NbHM, pregnant uterus
                     NbHPU, and fetal heart NbHH19W) were mixed, and ss circles
                     were made in vitro. Following HAP purification, this DNA
                     was used as tracer in a subtractive hybridization
                     reaction. The driver was PCR-amplified cDNAs from pools of
                     5,000 clones made from the same 3 libraries. The pools
                     consisted of I.M.A.G.E. clones 260232-265223,
                     340488-345479, and 484488-489479."
BASE COUNT       80 a     83 c     94 g     98 t
ORIGIN


  Query Match             23.6%;  Score 353.4;  DB 9;  Length 355;
  Best Local Similarity   99.7%;  Pred. No. 1.5e-86;
  Matches  354;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy    734 ccaccgctctcactatgatcctccaccaagccgacaggctggaggtctgtcccgctttcc 793
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    355 CCACCGCTCTCACTATGATCCTCCACCAAGCCGACAGGCTGGAGGTCTGTCCCGCTTTCC 296

Qy    794 tggggccagaagtcaccggggagctcttatggattcccagcaagcatcaggaaccattgt 853
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    295 TGGGGCCAGAAGTCACCGGGGAGCTCTTATGGATTCCCAGCAAGCATCAGGAACCATTGT 236

Qy    854 gcaaattgtcatcaataacaaacacaagcatggacaagtgtgtgtttccaatggaaagac 913
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    235 GCAAATTGTCATCAATAACAAACACAAGCATGGACAAGTGTGTGTTTCCAATGGAAAGAC 176

Qy    914 ctattctcatggcgagtcctggcacccaaacctccgggcatttggcattgtggagtgtgt 973
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    175 CTATTCTCATGGCGAGTCCTGGCACCCAAACCTCCGGGCATTTGGCATTGTGGAGTGTGT 116

Qy    974 gctatgtacttgtaatgtcaccaagcaagagtgtaagaaaatccactgccccaatcgata 1033
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    115 GCTATGTACTTGTAATGTCACCAAGCAAGAGTGTAAGAAAATCCACTGCCCCAATCGATA 56

Qy   1034 cccctgcaagtatcctcaaaaaatagacggaaagtgctgcaaggtgtgtccaggt 1088
          |||||||||||||||||||||||||||||| ||||||||||||||||||||
Db     55 CCCCTGCAAGTATCCTCAAAAAATAGACGGAAAATGCTGCAAGGTGTGTCCAGGT 1
```

Insofar as the isolated nucleic acid molecule was cloned then IMAGE clone 1857913 comprises the complement of the isolated nucleic acid molecule. The I.M.A.G.E. Consortium (v13) indicates that IMAGE clone 1857913 was available to the public on 12/14/98 (page 13). The nucleotide sequence that is 99.7% identical to nucleotides 734 - 1088 of the present application's SEQ ID NO: 7, or the complement thereof, hybridizes as set forth in 1(d), 2(e), or 3(g), in the absence of evidence to the contrary. The metes and bounds of "complementary" are not clearly set forth. The nucleotide sequence that is 99.7% identical to nucleotides 734 - 1088 of the present application's SEQ ID NO: 7, or the complement thereof, is "complementary" as set forth in 1(e), 2(f), or 3 (h). The nucleotide sequence that is 99.7% identical to nucleotides

734 - 1088 of the present application's SEQ ID NO: 7, or the complement thereof, comprises a region of the nucleotide sequence of SEQ ID NO: 7 or the ATCC Deposit No. that corresponds to SEQ ID NO: 7 that encodes a polypeptide fragment of at least about 25 amino acid residues, as indicated below:

```
alignment_scores:
           Quality:  118.00              Length:    118
             Ratio:  1.000                 Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-724-915-8 x AI246227/rev   ..

 Align seg 1/1  to reverse of: AI246227  from: 1  to: 355

     202 HisArgSerHisTyrAspProProProSerArgGlnAlaGlyGlyLeuSe 218
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     354 CACCGCTCTCACTATGATCCTCCACCAAGCCGACAGGCTGGAGGTCTGTC 305

     218 rArgPheProGlyAlaArgSerHisArgGlyAlaLeuMetAspSerGlnG 235
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     304 CCGCTTTCCTGGGGCCAGAAGTCACCGGGGAGCTCTTATGGATTCCCAGC 255

     235 lnAlaSerGlyThrIleValGlnIleValIleAsnAsnLysHisLysHis 251
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     254 AAGCATCAGGAACCATTGTGCAAATTGTCATCAATAACAAACACAAGCAT 205

     252 GlyGlnValCysValSerAsnGlyLysThrTyrSerHisGlyGluSerTr 268
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     204 GGACAAGTGTGTGTTTCCAATGGAAAGACCTATTCTCATGGCGAGTCCTG 155

     268 pHisProAsnLeuArgAlaPheGlyIleValGluCysValLeuCysThrC 285
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     154 GCACCCAAACCTCCGGGCATTTGGCATTGTGGAGTGTGTGCTATGTACTT 105

     285 ysAsnValThrLysGlnGluCysLysLysIleHisCysProAsnArgTyr 301
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     104 GTAATGTCACCAAGCAAGAGTGTAAGAAAATCCACTGCCCCAATCGATAC 55

     302 ProCysLysTyrProGlnLysIleAspGlyLysCysCysLysValCysPr 318
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      54 CCCTGCAAGTATCCTCAAAAAATAGACGGAAAATGCTGCAAGGTGTGTCC 5

     318 oGly 319
         ||||
       4 AGGT 1.
```

The metes and bounds of "an activity of the encoded polypeptide" are not clearly set forth. The polypeptide fragment has an activity of the encoded polypeptide set forth in SEQ ID NO: 8 or is antigenic, in the absence of evidence to the contrary. The nucleotide sequence that is 99.7% identical to nucleotides 734 - 1088 of the present application's SEQ ID NO: 7 comprises a region, as set forth in 2(d), or a nucleotide sequence comprising a fragment, as set forth in 3(f), as indicated above. The nucleotide sequence that is 99.7% identical to nucleotides 734 - 1088 of the present application's SEQ ID NO: 7 comprises a nucleotide sequence encoding a polypeptide as set forth in 3(c), 3(d) or 3(e). The metes and bounds of "an activity of the encoded

polypeptide" are not clearly set forth. The polypeptide fragment has an activity of the encoded polypeptide set forth in SEQ ID NO: 8, in the absence of evidence to the contrary.

The ability to determine percent identity by a given computer program or algorithm is viewed as a product-by-process limitation. The recitation of a process limitation is not viewed as positively limiting the claimed product absent a showing that the process imparts a novel property to the claimed product, as it is assumed that equivalent products are obtainable by multiple computer programs. The metes and bounds of "an activity of the encoded polypeptide" are not clearly set forth. The polypeptide or fragment thereof has an activity of the encoded polypeptide set forth in SEQ ID NO: 8 or is antigenic, in the absence of evidence to the contrary.

Claims 1-5, 7, 11 are rejected under 35 U.S.C. 102(a) as being anticipated by NCI-CGAP (u13).

The disclosure of NCI-CGAP (u13) discussed above is incorporated herein by reference. The structural and/or functional limitations of the nucleotide sequence that is 99.7% identical to nucleotides 734 - 1088 of the present application's SEQ ID NO: 7 as discussed above is incorporated herein by reference. NCI-CGAP (u13) discloses the vector pT7T3D-Pac comprising IMAGE clone 1857913 and the prokaryotic host cell DH10B comprising the vector.

Claims 1-5, 7, 11, 45 are rejected under 35 U.S.C. 102(a) as being anticipated by Jacobs (10, cited by Applicants). Jacobs discloses an isolated nucleic acid molecule (SEQ ID NO: 75) 99.7% identical to nucleotides 44-1495 of the present application's SEQ ID NO: 7, which

encodes a polypeptide (SEQ ID NO: 76) 99.8% identical to the present application's SEQ ID NO: 8, as indicated below:

```
AAZ33353
ID   AAZ33353 standard; cDNA; 3861 BP.
XX
AC   AAZ33353;
XX
DT   29-FEB-2000  (first entry)
XX
DE   Human secreted protein clone dw665_4 nucleotide sequence SEQ ID NO:75.
XX
KW   Human; secreted protein; nutritional; cytokine; cell proliferation;
KW   differentiation; immune stimulating; vaccine; suppression;
KW   haematopoiesis regulation; tissue growth; activin; inhibin;
KW   chemotactic; chemokinetic; haemostatic; thrombolytic; receptor;
KW   ligand; anti-inflammatory; cadherin; tumour invasion suppressor;
KW   tumour inhibition; gene therapy; ss.
XX
OS   Homo sapiens.
XX
PN   WO9957132-A1.
XX
PD   11-NOV-1999.
XX
PF   07-MAY-1999;   99WO-US09970.
XX
PR   07-MAY-1998;   98US-0084564.
PR   02-JUN-1998;   98US-0087645.
PR   22-JUL-1998;   98US-0093712.
PR   31-JUL-1998;   98US-0094935.
PR   10-AUG-1998;   98US-0095880.
PR   11-AUG-1998;   98US-0096068.
PR   06-MAY-1999;   99US-0096068.
XX
PA   (GEMY ) GENETICS INST INC.
XX
PI   Jacobs K,  McCoy JM,  LaVallie ER,  Collins-Racie LA,  Evans C;
PI   Merberg D,  Treacy M,  Agostino MJ,  Steininger RJ,  Bowman MR;
PI   DiBlasio-Smith E,  Widom A;
XX
DR   WPI; 2000-052937/04.
DR   P-PSDB; AAY53035.
XX
PT   New polynucleotides encoding secreted human proteins, derived from
PT   adult placenta, adult retina, fetal brain, fetal  -
XX
PS   Claim 84; Page 429-430; 492pp; English.
XX
CC   The present invention describes new human secreted proteins which were
CC   isolated from adult placenta, adult retina, foetal brain, foetal kidney,
CC   adult blood, adult brain, adult thyroid, adult bladder, adult neural
CC   tissue, adult testes, and adult lymph node cDNA libraries. The human
CC   secreted proteins, and the polynucleotides encoding them, are predicted
CC   to have biological activities which would make them suitable for
CC   treating, preventing or ameliorating medical conditions in humans and
CC   animals. Suggested activities include nutritional activity, cytokine
CC   and cell proliferation/differentiation activity, immune stimulating
CC   (e.g. as vaccines) or suppressing activity, haematopoiesis regulating
CC   activity, tissue growth activity, activin/inhibin activity,
CC   chemotactic/chemokinetic activity, haemostatic and thrombolytic
CC   activity, receptor/ligand activity, anti-inflammatory activity,
CC   cadherin/tumour invasion suppressor activity, and tumour inhibition
CC   activity. The polynucleotides are also stated to be useful for gene
CC   therapy. AAZ33316 to AAZ33373 encode human secreted proteins, and
CC   AAY52998 to AAY53060 represent human secreted proteins, given in the
CC   present invention.
XX
SQ   Sequence 3861 BP; 1158 A; 797 C; 853 G; 1053 T; 0 other;

  Query Match             95.9%;  Score 1434.4;  DB 21;  Length 3861;
  Best Local Similarity   99.7%;  Pred. No. 0;
  Matches 1448;  Conservative    0;  Mismatches    1;  Indels    3;  Gaps    1;

Qy     44 gtgcacgcgtggcagacggagaaggccagtgcccagcttgaaggttctgccacctttgc 103
          ||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||||
Db      1 gtgcacgcgtggcagacggagaaggccagtgcccagcttgaaggttctgtcacctttgc 60

Qy    104 agtggtccaaatgagaaaaaagtggaaaatgggaggcatgaaatacatcttttcgttgtt 163
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 agtggtccaaatgagaaaaaagtggaaaatgggaggcatgaaatacatcttttcgttgtt 120

Qy    164 gttctttctttgctagaaggaggcaaaacagagcaagtaaaacattcagagacatattg 223
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
Db    121 gttctttcttttgctagaaggaggcaaaacagagcaagtaaaacattcagagacatattg 180

Qy    224 catgtttcaagacaagaagtacagagtgggtgagagatggcatccttacctggaacctta 283
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 catgtttcaagacaagaagtacagagtgggtgagagatggcatccttacctggaacctta 240

Qy    284 tgggttggtttactgcgtgaactgcatctgctcagagaatgggaatgtgctttgcagccg 343
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 tgggttggtttactgcgtgaactgcatctgctcagagaatgggaatgtgctttgcagccg 300

Qy    344 agtcagatgtccaaatgttcattgcctttctcctgtgcatattcctcatctgtgctgccc 403
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 agtcagatgtccaaatgttcattgcctttctcctgtgcatattcctcatctgtgctgccc 360

Qy    404 tcgctgcccagaagactccttacccccagtgaacaataaggtgaccagcaagtcttgcga 463
          |||||||||  ||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 tcgctgccc---agactccttacccccagtgaacaataaggtgaccagcaagtcttgcga 417

Qy    464 gtacaatgggacaacttaccaacatggagagctgttcgtagctgaagggctctttcagaa 523
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    418 gtacaatgggacaacttaccaacatggagagctgttcgtagctgaagggctctttcagaa 477

Qy    524 tcggcaacccaatcaatgcacccagtgcagctgttcggagggaaacgtgtattgtggtct 583
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    478 tcggcaacccaatcaatgcacccagtgcagctgttcggagggaaacgtgtattgtggtct 537

Qy    584 caagacttgccccaaattaacctgtgccttcccagtctctgttccagattcctgctgccg 643
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    538 caagacttgccccaaattaacctgtgccttcccagtctctgttccagattcctgctgccg 597

Qy    644 ggtatgcagaggagatggagaactgtcatgggaacattctgatggtgatatcttccggca 703
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    598 ggtatgcagaggagatggagaactgtcatgggaacattctgatggtgatatcttccggca 657

Qy    704 acctgccaacagagaagcaagacattcttaccaccgctctcactatgatcctccaccaag 763
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    658 acctgccaacagagaagcaagacattcttaccaccgctctcactatgatcctccaccaag 717

Qy    764 ccgacaggctggaggtctgtcccgctttcctggggccagaagtcaccggggagctcttat 823
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    718 ccgacaggctggaggtctgtcccgctttcctggggccagaagtcaccggggagctcttat 777

Qy    824 ggattcccagcaagcatcaggaaccattgtgcaaattgtcatcaataacaaacacaagca 883
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    778 ggattcccagcaagcatcaggaaccattgtgcaaattgtcatcaataacaaacacaagca 837

Qy    884 tggacaagtgtgtgtttccaatggaaagacctattctcatggcgagtcctggcacccaaa 943
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    838 tggacaagtgtgtgtttccaatggaaagacctattctcatggcgagtcctggcacccaaa 897

Qy    944 cctccgggcatttggcattgtggagtgtgtgctatgtacttgtaatgtcaccaagcaaga 1003
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    898 cctccgggcatttggcattgtggagtgtgtgctatgtacttgtaatgtcaccaagcaaga 957

Qy   1004 gtgtaagaaaatccactgccccaatcgataccctgcaagtatcctcaaaaaatagacgg 1063
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    958 gtgtaagaaaatccactgccccaatcgataccctgcaagtatcctcaaaaaatagacgg 1017

Qy   1064 aaagtgctgcaaggtgtgtccaggtaaaaaagcaaaagaagaacttccaggccaaagctt 1123
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1018 aaagtgctgcaaggtgtgtccaggtaaaaaagcaaaagaagaacttccaggccaaagctt 1077

Qy   1124 tgacaataaaggctacttctgcggggaagaaacgatgcctgtgtatgagtctgtattcat 1183
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1078 tgacaataaaggctacttctgcggggaagaaacgatgcctgtgtatgagtctgtattcat 1137

Qy   1184 ggaggatggggagacaaccagaaaaatagcactggagactgagagaccacctcaggtaga 1243
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1138 ggaggatggggagacaaccagaaaaatagcactggagactgagagaccacctcaggtaga 1197

Qy   1244 ggtccacgtttggactattcgaaagggcattctccagcacttccatattgagaagatctc 1303
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1198 ggtccacgtttggactattcgaaagggcattctccagcacttccatattgagaagatctc 1257

Qy   1304 caagaggatgtttgaggagcttcctcacttcaagctggtgaccagaacaaccctgagcca 1363
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1258 caagaggatgtttgaggagcttcctcacttcaagctggtgaccagaacaaccctgagcca 1317

Qy   1364 gtggaagatcttcaccgaaggagaagctcagatcagccagatgtgttcaagtcgtgtatg 1423
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1318 gtggaagatcttcaccgaaggagaagctcagatcagccagatgtgttcaagtcgtgtatg 1377

Qy   1424 cagaacagagcttgaagatttagtcaaggttttgtacctggagagatctgaaaagggcca 1483
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1378 cagaacagagcttgaagatttagtcaaggttttgtacctggagagatctgaaaagggcca 1437

Qy   1484 ctgttaggcaag 1495
          ||||||||||||
Db   1438 ctgttaggcaag 1449
```

```
AAY53035
ID   AAY53035 standard; Protein; 457 AA.
XX
AC   AAY53035;
XX
DT   29-FEB-2000  (first entry)
XX
DE   Human secreted protein clone dw665_4 protein sequence SEQ ID NO:76.
XX
KW   Human; secreted protein; nutritional; cytokine; cell proliferation;
KW   differentiation; immune stimulating; vaccine; suppression;
KW   haematopoiesis regulation; tissue growth; activin; inhibin;
KW   chemotactic; chemokinetic; haemostatic; thrombolytic; receptor;
KW   ligand; anti-inflammatory; cadherin; tumour invasion suppressor;
KW   tumour inhibition; gene therapy.
XX
OS   Homo sapiens.
XX
PN   WO9957132-A1.
XX
PD   11-NOV-1999.
XX
PF   07-MAY-1999;   99WO-US09970.
XX
PR   07-MAY-1998;   98US-0084564.
PR   02-JUN-1998;   98US-0087645.
PR   22-JUL-1998;   98US-0093712.
PR   31-JUL-1998;   98US-0094935.
PR   10-AUG-1998;   98US-0095880.
PR   11-AUG-1998;   98US-0096068.
PR   06-MAY-1999;   99US-0096068.
XX
PA   (GEMY ) GENETICS INST INC.
XX
PI   Jacobs K,  McCoy JM,  LaVallie ER,  Collins-Racie LA,  Evans C;
PI   Merberg D,  Treacy M,  Agostino MJ,  Steininger RJ,  Bowman MR;
PI   DiBlasio-Smith E,  Widom A;
XX
DR   WPI; 2000-052937/04.
DR   N-PSDB; AAZ33353.
XX
PT   New polynucleotides encoding secreted human proteins, derived from
PT   adult placenta, adult retina, fetal brain, fetal  -
XX
PS   Claim 85; Page 430-432; 492pp; English.
XX
CC   The present invention describes new human secreted proteins which were
CC   isolated from adult placenta, adult retina, foetal brain, foetal kidney,
CC   adult blood, adult brain, adult thyroid, adult bladder, adult neural
CC   tissue, adult testes, and adult lymph node cDNA libraries. The human
CC   secreted proteins, and the polynucleotides encoding them, are predicted
CC   to have biological activities which would make them suitable for
CC   treating, preventing or ameliorating medical conditions in humans and
CC   animals. Suggested activities include nutritional activity, cytokine
CC   and cell proliferation/differentiation activity, immune stimulating
CC   (e.g. as vaccines) or suppressing activity, haematopoiesis regulating
CC   activity, tissue growth activity, activin/inhibin activity,
CC   chemotactic/chemokinetic activity, haemostatic and thrombolytic
CC   activity, receptor/ligand activity, anti-inflammatory activity,
CC   cadherin/tumour invasion suppressor activity, and tumour inhibition
CC   activity. The polynucleotides are also stated to be useful for gene
CC   therapy. AAZ33316 to AAZ33373 encode human secreted proteins, and
CC   AAY52998 to AAY53060 represent human secreted proteins, given in the
CC   present invention.
XX
SQ   Sequence   457 AA;


  Query Match             99.4%;  Score 2520.5;  DB 21;  Length 457;
  Best Local Similarity   99.8%;  Pred. No. 3.1e-184;
  Matches  451;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy       1 MGGMKYIFSLLFFLLLEGGKTEQVKHSETYCMFQDKKYRVGERWHPYLEPYGLVYCVNCI 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       7 mggmkyifsllffllleggkteqvkhsetycmfqdkkyrvgerwhpylepyglvycvnci 66

Qy      61 CSENGNVLCSRVRCPNVHCLSPVHIPHLCCPRCPEDSLPPVNNKVTSKSCEYNGTTYQHG 120
           ||||||||||||||||||||||||||||||| ||||||||||||||||||||||||||||
Db      67 csengnvlcsrvrcpnvhclspvhiphlccprcp-dslppvnnkvtsksceyngttyqhg 125

Qy     121 ELFVAEGLFQNRQPNQCTQCSCSEGNVYCGLKTCPKLTCAFPVSVPDSCCRVCRGDGELS 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     126 elfvaeglfqnrqpnqctqcscsegnvycglktcpkltcafpvsvpdsccrvcrgdgels 185

Qy     181 WEHSDGDIFRQPANREARHSYHRSHYDPPPSRQAGGLSRFPGARSHRGALMDSQQASGTI 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     186 wehsdgdifrqpanrearhsyhrshydpppsrqagglsrfpgarshrgalmdsqqasgti 245

Qy     241 VQIVINNKHKHGQVCVSNGKTYSHGESWHPNLRAFGIVECVLCTCNVTKQECKKIHCPNR 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db    246 vqivinnkhkhgqvcvsngktyshgeswhpnlrafgivecvlctcnvtkqeckkihcpnr 305

Qy    301 YPCKYPQKIDGKCCKVCPGKKAKEELPGQSFDNKGYFCGEETMPVYESVFMEDGETTRKI 360
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    306 ypckypqkidgkcckvcpgkkakeelpgqsfdnkgyfcgeetmpvyesvfmedgettrki 365

Qy    361 ALETERPPQVEVHVWTIRKGILQHFHIEKISKRMFEELPHFKLVTRTTLSQWKIFTEGEA 420
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    366 aleterppqvevhvwtirkgilqhfhiekiskrmfeelphfklvtrttlsqwkiftegea 425

Qy    421 QISQMCSSRVCRTELEDLVKVLYLERSEKGHC 452
          |||||||||||||||||||||||||||||||
Db    426 qisqmcssrvcrteledlvkvlylersekghc 457.
```

Jacobs also teaches polynucleotides encoding fragments of eight, i.e., "at least about 25", or thirty amino acids, ~~amino acid~~ a polynucleotide which is an allelic variant, a polynucleotide that hybridizes under stringent conditions, polynucleotides linked to an expression control sequence, suitable host cells for the expression of the protein, transformed host cells, recombinant methods of producing the protein, viral vectors comprising the polynucleotides (page 118, line 6, through page 121, line 12; page 264, line 14, through page 267, line 2; page 292, line 8). The ability to determine percent identity by a given computer program or algorithm is viewed as a product-by-process limitation. The recitation of a process limitation is not viewed as positively limiting the claimed product absent a showing that the process imparts a novel property to the claimed product, as it is assumed that equivalent products are obtainable by multiple computer programs. The metes and bounds of "an activity of the encoded polypeptide" are not clearly set forth. The polypeptide or fragment thereof has an activity of the encoded polypeptide set forth in SEQ ID NO: 8 or is antigenic, in the absence of evidence to the contrary. The metes and bounds of "CHL polypeptide" are not clearly set forth. The polypeptide encoded by the isolated nucleic acid molecule is a "CHL polypeptide" in the absence of evidence to the contrary. The polypeptide has an additional six amino acids at the N-terminus. The isolated nucleic acid molecule encodes an allelic variant or splice variant of SEQ ID NO: 7 or the ATCC Deposit No. that corresponds to SEQ ID NO: 7. Jacob's isolated nucleic acid molecules and/or

the complements thereof fall within the ambit of claims 1(d), 1(e), 2(a), 2(b), 2(c), 2(d), 2(e), 2(f), 3(a), 3(b), 3(c), 3(d), 3(e), 3(f), 3(g), 3(h).

Claims 3-8, 10, 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Nathans (a8). Embodiments 3(e), 3(f), 3(g), 3(h) of the present invention encompass essentially any and/or all nucleic acid molecules encoding any and/or all polypeptides. Nathans teaches an isolated nucleic acid molecule encoding a polypeptide, a viral vector comprising the nucleic acid molecule, eukaryotic and prokaryotic host cells comprising the vector, and methods of making the encoded polypeptide (Figure 1; column 6, last full paragraph; column 7, full paragraphs 1-3; column 12, full paragraph 2).

Claims 1-8, 10, 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Ruben (11, cited by Applicants). Ruben discloses a isolated nucleic acid molecule (SEQ ID NO: 47), or the complement thereof, that is 98.7% identical to the present application's SEQ ID NO: 7 and that encodes amino acids 21-318 of the present application's SEQ ID NO: 8, as indicated below:

```
AAV34322/c
ID   AAV34322 standard; DNA; 2315 BP.
XX
AC   AAV34322;
XX
DT   29-JAN-1999  (first entry)
XX
DE   Human secreted protein gene 20 clone HSDEG01.
XX
KW   Human; secreted protein; fusion protein; gene therapy; protein therapy;
KW   diagnosis; tissue; cancer; tumour; neurodegenerative disorder; leukaemia;
KW   developmental abnormality; foetal deficiency; blood; allergy; renal; ds;
KW   immune system; asthma; lymphocytic disease; brain; hepatic; lymphoma;
KW   inflammation; ischaemic shock; Alzheimer's disease; restenosis; AIDS;
KW   cognitive disorder; schizophrenia; prostate; obesity; osteoclast; thymus;
KW   osteoporosis; arthritis; testis; lung; thyroiditis; thyroid; digestion;
KW   endocrine; metabolism; regulation; malabsorption; gastritis; neoplasm.
XX
OS   Homo sapiens.
XX
PN   WO9840483-A2.
XX
PD   17-SEP-1998.
XX
PF   12-MAR-1998;   98WO-US04858.
XX
PR   19-DEC-1997;   97US-0068368.
PR   14-MAR-1997;   97US-0040710.
PR   14-MAR-1997;   97US-0040762.
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PR   30-MAY-1997;   97US-0048100.
PR   30-MAY-1997;   97US-0048189.
PR   30-MAY-1997;   97US-0048357.
PR   30-MAY-1997;   97US-0050934.
PR   06-JUN-1997;   97US-0048970.
PR   05-SEP-1997;   97US-0057765.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
XX
PI   Ferrie AM,  Fischer CL,  Gentz RL,  Greene JM,  Kyaw H;
PI   Li H,  Li Y,  Moore PA,  Rosen CA,  Ruben SM,  Soppet DR;
PI   Wei YF,  Young PE,  Zeng Z;
XX
DR   WPI; 1998-520811/44.
DR   P-PSDB; AAW75232.
XX
PT   Isolated human poly:nucleotide(s) encoding secretory peptide(s) -
PT   used to develop products for the diagnosis and treatment of e.g.
PT   inflammation, cancers, CNS disorders or immune system disorders
XX
PS   Claim 1; Page 148-149; 201pp; English.
XX
CC   This sequence represents a nucleic acid molecule which encodes a
CC   secreted human protein.  The gene number, and the clone it is derived
CC   from, are detailed in the descriptor line.  The gene can be used to
CC   generate fusion proteins by linking to the gene to a human immunoglobulin
CC   Fc portion (e.g. AAV34277) for increasing the stability of the fused
CC   protein as compared to the human protein only.
CC   The invention relates to 28 novel genes and their fragments (nucleic
CC   acid sequences: AAV34286-V34325; amino acid sequences AAW75196-W75235)
CC   which are useful for preventing, treating or ameliorating  medical
CC   conditions e.g. by protein or gene therapy.  Also, pathological
CC   conditions can be diagnosed by determining the amount of the new
CC   polypeptides in a sample or by determining the presence of mutations in
CC   the new polynucleotides. Specific uses are described for each of the 28
CC   polynucleotides, based on which tissues they are most highly expressed in
CC   (see AAV34286 for described uses).
XX
SQ   Sequence 2315 BP; 582 A; 562 C; 510 G; 657 T; 4 other;

  Query Match             86.0%;  Score 1287;  DB 19;  Length 2315;
  Best Local Similarity   98.7%;  Pred. No. 0;
  Matches 1312;  Conservative    1;  Mismatches    1;  Indels   15;  Gaps    1;

Qy     167 ctttcttttgctagaaggaggcaaaacagagcaagtaaaacattcagagacatattgcat 226
           ||||||||||||||||||||||:||||||||||||||||||||||||||||||||||||
Db    2107 CTTTCTTTTGCTAGAAGGAGGCMAAACAGAGCAAGTAAAACATTCAGAGACATATTGCAT 2048

Qy     227 gtttcaagacaagaagtacagagtgggtgagagatggcatccttacctggaaccttatgg 286
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2047 GTTTCAAGACAAGAAGTACAGAGTGGGTGAGAGATGGCATCCTTACCTGGAACCTTATGG 1988

Qy     287 gttggtttactgcgtgaactgcatctgctcagagaatgggaatgtgctttgcagccgagt 346
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1987 GTTGGTTTACTGCGTGAACTGCATCTGCTCAGAGAATGGGAATGTGCTTTGCAGCCGAGT 1928

Qy     347 cagatgtccaaatgttcattgcctttctcctgtgcatattcctcatctgtgctgccctcg 406
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1927 CAGATGTCCAAATGTTCATTGCCTTTCTCCTGTGCATATTCCTCATCTGTGCTGCCCTCG 1868

Qy     407 ctgcccagaagactccttacccccagtgaacaataaggtgaccagcaagtcttgcgagta 466
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1867 CTGCCCAGAAGACTCCTTACCCCCAGTGAACAATAAGGTGACCAGCAAGTCTTGCGAGTA 1808

Qy     467 caatgggacaacttaccaacatggagagctgttcgtagctgaagggctctttcagaatcg 526
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1807 CAATGGGACAACTTACCAACATGGAGAGCTGTTCGTAGCTGAAGGGCTCTTTCAGAATCG 1748

Qy     527 gcaacccaatcaatgcacccagtgcagctgttcggagggaaacgtgtattgtggtctcaa 586
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1747 GCAACCCAATCAATGCACCCAGTGCAGCTGTTCGGAGGGAAACGTGTATTGTGGTCTCAA 1688

Qy     587 gacttgccccaaattaacctgtgccttcccagtctctgttccagattcctgctgccgggt 646
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1687 GACTTGCCCCAAATTAACCTGTGCCTTCCCAGTCTCTGTTCCAGATTCCTGCTGCCGGGT 1628

Qy     647 atgcagaggagatggagaactgtcatgggaacattctgatggtgatatcttccggcaacc 706
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1627 ATGCAGAGGAGATGGAGAACTGTCATGGGAACATTCTGATGGTGATATCTTCCGGCAACC 1568

Qy     707 tgccaacagagaagcaagacattcttaccaccgctctcactatgatcctccaccaagccg 766
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1567 TGCCAACAGAGAAGCAAGACATTCTTACCACCGCTCTCACTATGATCCTCCACCAAGCCG 1508

Qy     767 acaggctggaggtctgtcccgctttcctggggccagaagtcaccggggagctcttatgga 826
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1507 ACAGGCTGGAGGTCTGTCCCGCTTTCCTGGGGCCAGAAGTCACCGGGGAGCTCTTATGGA 1448

Qy     827 ttcccagcaagcatcaggaaccattgtgcaaattgtcatcaataacaaacacaagcatgg 886
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              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1447 TTCCCAGCAAGCATCAGGAACCATTGTGCAAATTGTCATCAATAACAAACACAAGCATGG 1388

Qy     887 acaagtgtgtgtttccaatggaaagacctattctcatggcgagtcctggcacccaaacct 946
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1387 ACAAGTGTGTGTTTCCAATGGAAAGACCTATTCTCATGGCGAGTCCTGGCACCCAAACCT 1328

Qy     947 ccgggcatttggcattgtggagtgtgtgctatgtacttgtaatgtcaccaagcaagagtg 1006
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1327 CCGGGCATTTGGCATTGTGGAGTGTGTGCTATGTACTTGTAATGTCACCAAGCAAGAGTG 1268

Qy    1007 taagaaaatccactgccccaatcgataccctgcaagtatcctcaaaaaatagacggaaa 1066
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1267 TAAGAAAATCCACTGCCCCAATCGATACCCCTGCAAGTATCCTCAAAAAATAGACGGAAA 1208

Qy    1067 gtgctgcaaggtgtgtccaggtaaaaaagcaaaagaagaacttccaggccaaagctttga 1126
              ||||||||||||||||||              ||||||||||||||||||||||||||||||
Db    1207 ATGCTGCAAGGTGTGTCC----------------AGAAGAACTTCCAGGCCAAAGCTTTGA 1163

Qy    1127 caataaaggctacttctgcggggaagaaacgatgcctgtgtatgagtctgtattcatgga 1186
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1162 CAATAAAGGCTACTTCTGCGGGGAAGAAACGATGCCTGTGTATGAGTCTGTATTCATGGA 1103

Qy    1187 ggatggggagacaaccagaaaaatagcactggagactgagagaccacctcaggtagaggt 1246
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1102 GGATGGGGAGACAACCAGAAAAATAGCACTGGAGACTGAGAGACCACCTCAGGTAGAGGT 1043

Qy    1247 ccacgtttggactattcgaaagggcattctccagcacttccatattgagaagatctccaa 1306
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1042 CCACGTTTGGACTATTCGAAAGGGCATTCTCCAGCACTTCCATATTGAGAAGATCTCCAA 983

Qy    1307 gaggatgtttgaggagcttcctcacttcaagctggtgaccagaacaaccctgagccagtg 1366
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     982 GAGGATGTTTGAGGAGCTTCCTCACTTCAAGCTGGTGACCAGAACAACCCTGAGCCAGTG 923

Qy    1367 gaagatcttcaccgaaggagaagctcagatcagccagatgtgttcaagtcgtgtatgcag 1426
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     922 GAAGATCTTCACCGAAGGAGAAGCTCAGATCAGCCAGATGTGTTCAAGTCGTGTATGCAG 863

Qy    1427 aacagagcttgaagatttagtcaaggttttgtacctggagagatctgaaaagggccactg 1486
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     862 AACAGAGCTTGAAGATTTAGTCAAGGTTTTGTACCTGGAGAGATCTGAAAAGGGCCACTG 803

Qy    1487 ttaggcaag 1495
              |||||||||
Db     802 TTAGGCAAG 794
```

ID AAV34322 standard; DNA; 2315 BP.
XX
AC AAV34322;
XX
DT 29-JAN-1999 (first entry)
XX
DE Human secreted protein gene 20 clone HSDEG01.
XX
KW Human; secreted protein; fusion protein; gene therapy; protein therapy;
KW diagnosis; tissue; cancer; tumour; neurodegenerative disorder; leukaemia;
KW developmental abnormality; foetal deficiency; blood; allergy; renal; ds;
KW immune system; asthma; lymphocytic disease; brain; hepatic; lymphoma;
KW inflammation; ischaemic shock; Alzheimer's disease; restenosis; AIDS;
KW cognitive disorder; schizophrenia; prostate; obesity; osteoclast; thymus;
KW osteoporosis; arthritis; testis; lung; thyroiditis; thyroid; digestion;
KW endocrine; metabolism; regulation; malabsorption; gastritis; neoplasm.
XX
OS Homo sapiens.
XX
PN WO9840483-A2.
XX
PD 17-SEP-1998.
XX
PF 12-MAR-1998; 98WO-US04858.
XX
PR 19-DEC-1997; 97US-0068368.
PR 14-MAR-1997; 97US-0040710.
PR 14-MAR-1997; 97US-0040762.
PR 30-MAY-1997; 97US-0048100.
PR 30-MAY-1997; 97US-0048189.
PR 30-MAY-1997; 97US-0048357.
PR 30-MAY-1997; 97US-0050934.
PR 06-JUN-1997; 97US-0048970.
PR 05-SEP-1997; 97US-0057765.
XX
PA (HUMA-) HUMAN GENOME SCI INC.
XX
PI Ferrie AM, Fischer CL, Gentz RL, Greene JM, Kyaw H;
PI Li H, Li Y, Moore PA, Rosen CA, Ruben SM, Soppet DR;
PI Wei YF, Young PE, Zeng Z;
XX
DR WPI; 1998-520811/44.

```
DR   P-PSDB; AAW75232.
XX
PT   Isolated human poly:nucleotide(s) encoding secretory peptide(s) -
PT   used to develop products for the diagnosis and treatment of e.g.
PT   inflammation, cancers, CNS disorders or immune system disorders
XX
PS   Claim 1; Page 148-149; 201pp; English.
XX
CC   This sequence represents a nucleic acid molecule which encodes a
CC   secreted human protein.  The gene number, and the clone it is derived
CC   from, are detailed in the descriptor line.  The gene can be used to
CC   generate fusion proteins by linking to the gene to a human immunoglobulin
CC   Fc portion (e.g. AAV34277) for increasing the stability of the fused
CC   protein as compared to the human protein only.
CC   The invention relates to 28 novel genes and their fragments (nucleic
CC   acid sequences: AAV34286-V34325; amino acid sequences AAW75196-W75235)
CC   which are useful for preventing, treating or ameliorating  medical
CC   conditions e.g. by protein or gene therapy.  Also, pathological
CC   conditions can be diagnosed by determining the amount of the new
CC   polypeptides in a sample or by determining the presence of mutations in
CC   the new polynucleotides. Specific uses are described for each of the 28
CC   polynucleotides, based on which tissues they are most highly expressed in
CC   (see AAV34286 for described uses).
XX
SQ   Sequence 2315 BP; 582 A; 562 C; 510 G; 657 T; 4 other;


alignment_scores:
            Quality:  298.00              Length:    298
              Ratio:  1.000                 Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-724-915-8 x AAV34322/rev   ..

 Align seg 1/1  to reverse of: AAV34322  from: 1  to: 2315

      21 ThrGluGlnValLysHisSerGluThrTyrCysMetPheGlnAspLysLy 37
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    2082 ACAGAGCAAGTAAAACATTCAGAGACATATTGCATGTTTCAAGACAAGAA 2033

      37 sTyrArgValGlyGluArgTrpHisProTyrLeuGluProTyrGlyLeuV 54
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    2032 GTACAGAGTGGGTGAGAGATGGCATCCTTACCTGGAACCTTATGGGTTGG 1983

      54 alTyrCysValAsnCysIleCysSerGluAsnGlyAsnValLeuCysSer 70
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1982 TTTACTGCGTGAACTGCATCTGCTCAGAGAATGGGAATGTGCTTTGCAGC 1933

      71 ArgValArgCysProAsnValHisCysLeuSerProValHisIleProHi 87
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1932 CGAGTCAGATGTCCAAATGTTCATTGCCTTTCTCCTGTGCATATTCCTCA 1883

      87 sLeuCysCysProArgCysProGluAspSerLeuProProValAsnAsnL 104
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1882 TCTGTGCTGCCCTCGCTGCCCAGAAGACTCCTTACCCCCAGTGAACAATA 1833

     104 ysValThrSerLysSerCysGluTyrAsnGlyThrThrTyrGlnHisGly 120
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1832 AGGTGACCAGCAAGTCTTGCGAGTACAATGGGACAACTTACCAACATGGA 1783

     121 GluLeuPheValAlaGluGlyLeuPheGlnAsnArgGlnProAsnGlnCy 137
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1782 GAGCTGTTCGTAGCTGAAGGGCTCTTTCAGAATCGGCAACCCAATCAATG 1733

     137 sThrGlnCysSerCysSerGluGlyAsnValTyrCysGlyLeuLysThrC 154
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1732 CACCCAGTGCAGCTGTTCGGAGGGAAACGTGTATTGTGGTCTCAAGACTT 1683

     154 ysProLysLeuThrCysAlaPheProValSerValProAspSerCysCys 170
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1682 GCCCCAAATTAACCTGTGCCTTCCCAGTCTCTGTTCCAGATTCCTGCTGC 1633

     171 ArgValCysArgGlyAspGlyGluLeuSerTrpGluHisSerAspGlyAs 187
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1632 CGGGTATGCAGAGGAGATGGAGAACTGTCATGGGAACATTCTGATGGTGA 1583

     187 pIlePheArgGlnProAlaAsnArgGluAlaArgHisSerTyrHisArgS 204
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1582 TATCTTCCGGCAACCTGCCAACAGAGAAGCAAGACATTCTTACCACCGCT 1533

     204 erHisTyrAspProProProSerArgGlnAlaGlyGlyLeuSerArgPhe 220
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1532 CTCACTATGATCCTCCACCAAGCCGACAGGCTGGAGGTCTGTCCCGCTTT 1483

     221 ProGlyAlaArgSerHisArgGlyAlaLeuMetAspSerGlnGlnAlaSe 237
         ||||||||||||||||||||||||||||||||||||||||||||||||||
    1482 CCTGGGGCCAGAAGTCACCGGGGAGCTCTTATGGATTCCCAGCAAGCATC 1433

     237 rGlyThrIleValGlnIleValIleAsnAsnLysHisLysHisGlyGlnV 254
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          ||||||||||||||||||||||||||||||||||||||||||||||||||
      1432 AGGAACCATTGTGCAAATTGTCATCAATAACAAACACAAGCATGGACAAG 1383

       254 alCysValSerAsnGlyLysThrTyrSerHisGlyGluSerTrpHisPro 270
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      1382 TGTGTGTTTCCAATGGAAAGACCTATTCTCATGGCGAGTCCTGGCACCCA 1333

       271 AsnLeuArgAlaPheGlyIleValGluCysValLeuCysThrCysAsnVa 287
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      1332 AACCTCCGGGCATTTGGCATTGTGGAGTGTGTGCTATGTACTTGTAATGT 1283

       287 lThrLysGlnGluCysLysLysIleHisCysProAsnArgTyrProCysL 304
          ||||||||||||||||||||||||||||||||||||||||||||||||||
      1282 CACCAAGCAAGAGTGTAAGAAAATCCACTGCCCCAATCGATACCCCTGCA 1233

       304 ysTyrProGlnLysIleAspGlyLysCysCysLysValCysPro 318
          |||||||||||||||||||||||||||||||||||||||||||
      1232 AGTATCCTCAAAAAATAGACGGAAAATGCTGCAAGGTGTGTCCA 1189.
```

Ruben also discloses an isolated nucleic acid molecule (SEQ ID NO: 30), or the complement thereof, that is 98% identical to the present application's SEQ ID NO: 7 and that encodes amino acids 157-318 of the present application's SEQ ID NO: 8, as indicated below:

```
AAV34305
ID   AAV34305 standard; DNA; 1732 BP.
XX
AC   AAV34305;
XX
DT   29-JAN-1999  (first entry)
XX
DE   Human secreted protein gene 20 clone HSDEG01.
XX
KW   Human; secreted protein; fusion protein; gene therapy; protein therapy;
KW   diagnosis; tissue; cancer; tumour; neurodegenerative disorder; leukaemia;
KW   developmental abnormality; foetal deficiency; blood; allergy; renal; ds;
KW   immune system; asthma; lymphocytic disease; brain; hepatic; lymphoma;
KW   inflammation; ischaemic shock; Alzheimer's disease; restenosis; AIDS;
KW   cognitive disorder; schizophrenia; prostate; obesity; osteoclast; thymus;
KW   osteoporosis; arthritis; testis; lung; thyroiditis; thyroid; digestion;
KW   endocrine; metabolism; regulation; malabsorption; gastritis; neoplasm.
XX
OS   Homo sapiens.
XX
PN   WO9840483-A2.
XX
PD   17-SEP-1998.
XX
PF   12-MAR-1998;   98WO-US04858.
XX
PR   19-DEC-1997;   97US-0068368.
PR   14-MAR-1997;   97US-0040710.
PR   14-MAR-1997;   97US-0040762.
PR   30-MAY-1997;   97US-0048100.
PR   30-MAY-1997;   97US-0048189.
PR   30-MAY-1997;   97US-0048357.
PR   30-MAY-1997;   97US-0050934.
PR   06-JUN-1997;   97US-0048970.
PR   05-SEP-1997;   97US-0057765.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
XX
PI   Ferrie AM,  Fischer CL,  Gentz RL,  Greene JM,  Kyaw H;
PI   Li H,  Li Y,  Moore PA,  Rosen CA,  Ruben SM,  Soppet DR;
PI   Wei YF,  Young PE,  Zeng Z;
XX
DR   WPI; 1998-520811/44.
DR   P-PSDB; AAW75215.
XX
PT   Isolated human poly:nucleotide(s) encoding secretory peptide(s) -
PT   used to develop products for the diagnosis and treatment of e.g.
PT   inflammation, cancers, CNS disorders or immune system disorders
XX
PS   Claim 1; Page 132-133; 201pp; English.
XX
CC   This sequence represents a nucleic acid molecule which encodes a
CC   secreted human protein.  The gene number, and the clone it is derived
CC   from, are detailed in the descriptor line.  The gene can be used to
CC   generate fusion proteins by linking to the gene to a human immunoglobulin
CC   Fc portion (e.g. AAV34277) for increasing the stability of the fused
```

```
CC   protein as compared to the human protein only.
CC   The invention relates to 28 novel genes and their fragments (nucleic
CC   acid sequences: AAV34286-V34325; amino acid sequences AAW75196-W75235)
CC   which are useful for preventing, treating or ameliorating medical
CC   conditions e.g. by protein or gene therapy. Also, pathological
CC   conditions can be diagnosed by determining the amount of the new
CC   polypeptides in a sample or by determining the presence of mutations in
CC   the new polynucleotides. Specific uses are described for each of the 28
CC   polynucleotides, based on which tissues they are most highly expressed in
CC   (see AAV34286 for described uses).
XX
SQ   Sequence 1732 BP; 507 A; 362 C; 418 G; 442 T; 3 other;

  Query Match             60.0%;  Score 897.2;  DB 19;  Length 1732;
  Best Local Similarity   98.0%;  Pred. No. 7.5e-270;
  Matches  921;  Conservative    3;  Mismatches    1;  Indels   15;  Gaps    1;

Qy    556 gttcggagggaaacgtgtattgtggtctcaagacttgccccaaattaacctgtgccttcc 615
          ||||||||||||||||||||||||||||||||::||||||:||||||||||||||||||
Db      1 gttcggagggaaacgtgtattgtggtctcaagmmttgccccawattaacctgtgccttcc 60

Qy    616 cagtctctgttccagattcctgctgccgggtatgcagaggagatggagaactgtcatggg 675
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 cagtctctgttccagattcctgctgccgggtatgcagaggagatggagaactgtcatggg 120

Qy    676 aacattctgatggtgatatcttccggcaacctgccaacagagaagcaagacattcttacc 735
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 aacattctgatggtgatatcttccggcaacctgccaacagagaagcaagacattcttacc 180

Qy    736 accgctctcactatgatcctccaccaagccgacaggctggaggtctgtcccgctttcctg 795
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 accgctctcactatgatcctccaccaagccgacaggctggaggtctgtcccgctttcctg 240

Qy    796 gggccagaagtcaccggggagctcttatggattcccagcaagcatcaggaaccattgtgc 855
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 gggccagaagtcaccggggagctcttatggattcccagcaagcatcaggaaccattgtgc 300

Qy    856 aaattgtcatcaataacaaacacaagcatggacaagtgtgtgtttccaatggaaagacct 915
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 aaattgtcatcaataacaaacacaagcatggacaagtgtgtgtttccaatggaaagacct 360

Qy    916 attctcatggcgagtcctggcacccaaacctccgggcatttggcattgtggagtgtgtgc 975
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 attctcatggcgagtcctggcacccaaacctccgggcatttggcattgtggagtgtgtgc 420

Qy    976 tatgtacttgtaatgtcaccaagcaagagtgtaagaaaatccactgccccaatcgatacc 1035
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 tatgtacttgtaatgtcaccaagcaagagtgtaagaaaatccactgccccaatcgatacc 480

Qy   1036 cctgcaagtatcctcaaaaaatagacggaaagtgctgcaaggtgtgtccaggtaaaaaag 1095
          |||||||||||||||||||||||||||||| ||||||||||||||||
Db    481 cctgcaagtatcctcaaaaaatagacggaaaatgctgcaaggtgtgtcc----------- 529

Qy   1096 caaaagaagaacttccaggccaaagctttgacaataaaggctacttctgcggggaagaaa 1155
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    530 ----agaagaacttccaggccaaagctttgacaataaaggctacttctgcggggaagaaa 585

Qy   1156 cgatgcctgtgtatgagtctgtattcatggaggatggggagacaaccagaaaaatagcac 1215
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    586 cgatgcctgtgtatgagtctgtattcatggaggatggggagacaaccagaaaaatagcac 645

Qy   1216 tggagactgagagaccacctcaggtagaggtccacgtttggactattcgaaagggcattc 1275
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    646 tggagactgagagaccacctcaggtagaggtccacgtttggactattcgaaagggcattc 705

Qy   1276 tccagcacttccatattgagaagatctccaagaggatgtttgaggagcttcctcacttca 1335
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    706 tccagcacttccatattgagaagatctccaagaggatgtttgaggagcttcctcacttca 765

Qy   1336 agctggtgaccagaacaaccctgagccagtggaagatcttcaccgaaggagaagctcaga 1395
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    766 agctggtgaccagaacaaccctgagccagtggaagatcttcaccgaaggagaagctcaga 825

Qy   1396 tcagccagatgtgttcaagtcgtgtatgcagaacagagcttgaagatttagtcaaggttt 1455
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    826 tcagccagatgtgttcaagtcgtgtatgcagaacagagcttgaagatttagtcaaggttt 885

Qy   1456 tgtacctggagagatctgaaaagggccactgttaggcaag 1495
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Db    886 tgtacctggagagatctgaaaagggccactgttaggcaag 925

ID   AAV34305 standard; DNA; 1732 BP.
XX
AC   AAV34305;
XX
DT   29-JAN-1999  (first entry)
XX
DE   Human secreted protein gene 20 clone HSDEG01.
```

```
XX
KW   Human; secreted protein; fusion protein; gene therapy; protein therapy;
KW   diagnosis; tissue; cancer; tumour; neurodegenerative disorder; leukaemia;
KW   developmental abnormality; foetal deficiency; blood; allergy; renal; ds;
KW   immune system; asthma; lymphocytic disease; brain; hepatic; lymphoma;
KW   inflammation; ischaemic shock; Alzheimer's disease; restenosis; AIDS;
KW   cognitive disorder; schizophrenia; prostate; obesity; osteoclast; thymus;
KW   osteoporosis; arthritis; testis; lung; thyroiditis; thyroid; digestion;
KW   endocrine; metabolism; regulation; malabsorption; gastritis; neoplasm.
XX
OS   Homo sapiens.
XX
PN   WO9840483-A2.
XX
PD   17-SEP-1998.
XX
PF   12-MAR-1998;   98WO-US04858.
XX
PR   19-DEC-1997;   97US-0068368.
PR   14-MAR-1997;   97US-0040710.
PR   14-MAR-1997;   97US-0040762.
PR   30-MAY-1997;   97US-0048100.
PR   30-MAY-1997;   97US-0048189.
PR   30-MAY-1997;   97US-0048357.
PR   30-MAY-1997;   97US-0050934.
PR   06-JUN-1997;   97US-0048970.
PR   05-SEP-1997;   97US-0057765.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
XX
PI   Ferrie AM,  Fischer CL,  Gentz RL,  Greene JM,  Kyaw H;
PI   Li H,  Li Y,  Moore PA,  Rosen CA,  Ruben SM,  Soppet DR;
PI   Wei YF,  Young PE,  Zeng Z;
XX
DR   WPI; 1998-520811/44.
DR   P-PSDB; AAW75215.
XX
PT   Isolated human poly:nucleotide(s) encoding secretory peptide(s) -
PT   used to develop products for the diagnosis and treatment of e.g.
PT   inflammation, cancers, CNS disorders or immune system disorders
XX
PS   Claim 1; Page 132-133; 201pp; English.
XX
CC   This sequence represents a nucleic acid molecule which encodes a
CC   secreted human protein.  The gene number, and the clone it is derived
CC   from, are detailed in the descriptor line.  The gene can be used to
CC   generate fusion proteins by linking to the gene to a human immunoglobulin
CC   Fc portion (e.g. AAV34277) for increasing the stability of the fused
CC   protein as compared to the human protein only.
CC   The invention relates to 28 novel genes and their fragments (nucleic
CC   acid sequences: AAV34286-V34325; amino acid sequences AAW75196-W75235)
CC   which are useful for preventing, treating or ameliorating  medical
CC   conditions e.g. by protein or gene therapy.  Also, pathological
CC   conditions can be diagnosed by determining the amount of the new
CC   polypeptides in a sample or by determining the presence of mutations in
CC   the new polynucleotides. Specific uses are described for each of the 28
CC   polynucleotides, based on which tissues they are most highly expressed in
CC   (see AAV34286 for described uses).
XX
SQ   Sequence 1732 BP; 507 A; 362 C; 418 G; 442 T; 3 other;


alignment_scores:
            Quality:  162.00              Length:    162
              Ratio:  1.000                 Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-724-915-8 x AAV34305    ..

 Align seg 1/1  to: AAV34305  from: 1  to: 1732

     157 LeuThrCysAlaPheProValSerValProAspSerCysCysArgValCy 173
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      45 TTAACCTGTGCCTTCCCAGTCTCTGTTCCAGATTCCTGCTGCCGGGTATG 94

     173 sArgGlyAspGlyGluLeuSerTrpGluHisSerAspGlyAspIlePheA 190
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      95 CAGAGGAGATGGAGAACTGTCATGGGAACATTCTGATGGTGATATCTTCC 144

     190 rgGlnProAlaAsnArgGluAlaArgHisSerTyrHisArgSerHisTyr 206
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     145 GGCAACCTGCCAACAGAGAAGCAAGACATTCTTACCACCGCTCTCACTAT 194

     207 AspProProProSerArgGlnAlaGlyGlyLeuSerArgPheProGlyAl 223
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     195 GATCCTCCACCAAGCCGACAGGCTGGAGGTCTGTCCCGCTTTCCTGGGGC 244

     223 aArgSerHisArgGlyAlaLeuMetAspSerGlnGlnAlaSerGlyThrI 240
         ||||||||||||||||||||||||||||||||||||||||||||||||||
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245 CAGAAGTCACCGGGGAGCTCTTATGGATTCCCAGCAAGCATCAGGAACCA 294

240 leValGlnIleValIleAsnAsnLysHisLysHisGlyGlnValCysVal 256
    ||||||||||||||||||||||||||||||||||||||||||||||||||
295 TTGTGCAAATTGTCATCAATAACAAACACAAGCATGGACAAGTGTGTGTT 344

257 SerAsnGlyLysThrTyrSerHisGlyGluSerTrpHisProAsnLeuAr 273
    ||||||||||||||||||||||||||||||||||||||||||||||||||
345 TCCAATGGAAAGACCTATTCTCATGGCGAGTCCTGGCACCCAAACCTCCG 394

273 gAlaPheGlyIleValGluCysValLeuCysThrCysAsnValThrLysG 290
    ||||||||||||||||||||||||||||||||||||||||||||||||||
395 GGCATTTGGCATTGTGGAGTGTGTGCTATGTACTTGTAATGTCACCAAGC 444

290 lnGluCysLysLysIleHisCysProAsnArgTyrProCysLysTyrPro 306
    ||||||||||||||||||||||||||||||||||||||||||||||||||
445 AAGAGTGTAAGAAAATCCACTGCCCCAATCGATACCCCTGCAAGTATCCT 494

307 GlnLysIleAspGlyLysCysCysLysValCysPro 318
    ||||||||||||||||||||||||||||||||||
495 CAAAAAATAGACGGAAAATGCTGCAAGGTGTGTCCA 530
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Ruben aslo discloses allelic variants (paragraph bridging pages 41-42), N- and C-terminal truncations of the encoded polypeptide (page 42, last full paragraph), polynucleotide and polypeptide fragments (pages 44-45), vectors, host cells, and protein production (pages 48-49). Ruben's isolated nucleic acid molecules and/or the complements thereof fall within the ambit of claims 1(d), 1(e), 2(a), 2(b), 2(c), 2(d), 2(e), 2(f), 3(a), 3(b), 3(c), 3(d), 3(e), 3(f), 3(g), 3(h).

Conclusion

No claims are allowable. SEQ ID NO: 7 and a polynucleotide encoding the amino acid sequence of SEQ ID NO: 8 are free of the prior art of record.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306
AFTER FINAL (703) 872-9307

IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
MARCH 18, 2003